

APPLICANTS: Comb *et al.*  
U.S.S.N.: 09/535,364

37. (New) A motif-specific, context-independent antibody that binds a motif consisting of a single acetylated amino acid, said antibody recognizing a plurality of peptides or proteins within a genome that contain said motif, wherein said antibody is produced by a method comprising the steps of:

- (a) constructing a combinatorial peptide library comprising (i) a fixed motif consisting of a single acetylated amino acid, and (ii) a plurality of degenerate amino acids surrounding said motif;
- (b) immunizing a host with said peptide library; and
- (c) isolating antisera from said host, and purifying said motif-specific, context-independent antibody from said antisera, said antibody recognizing a plurality of peptides or a proteins with a genome that contain said motif.

38. (New) The antibody of claim 37, wherein said acetylated amino acid is acetyl-lysine.

#### REMARKS

This Preliminary Amendment is being filed subsequent to a Notice of Allowance recently received in co-pending parent application, USSN 09/148,712, and is submitted, in part, to pursue subject matter disclosed but not claimed in the allowed parent application. Upon entry of the present amendments, claims 19, 21-22, and 27-38 are pending.

Applicants have amended the specification, on page 1, to recite the priority information claimed at the time of filing. 37 C.F.R. §1.78. Applicants have amended the claims, as indicated above, in order to voluntarily redefine the presently claimed subject matter. Claims 1-18, 20, and 23-26 have been cancelled; the subject matter of claims 9-11 and 23-26 being redefined in new claims 27-38. Lastly, claims 19 and 20-21 have been amended to voluntarily redefine the claimed subject matter. Support for these amendments is found throughout the specification, as originally filed, e.g. at p. 2, lines 6-18; p. 7, lines 19-23; p. 8, lines 16-22; p. 15, lines 6-14; p. 20, lines 3-7; and p. 24, line 16 to p. 26, line 11, and including the claims as originally filed. These amendments do not introduce new matter.

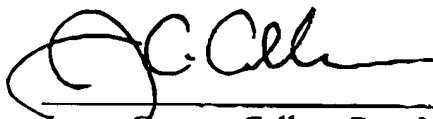
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Applicants' invention provides, in part, a novel class of antibodies that are both motif-specific and context-independent. The antibodies of the invention are designed for, and are capable of, recognizing short modified motifs -- e.g. kinase consensus substrate motifs, protein-protein binding motifs -- that occur in a plurality of peptides or proteins within a genome, such as motifs typically conserved among cell signaling proteins. These novel reagents enable, for the first time, methods for examining the modification of multiple proteins throughout a genome using a single antibody (see, e.g., specification at p. 21, lines 5-10), and thus solve the limitation of prior antibodies described in the Background of the Invention at p. 2-6. Accordingly, Applicants respectfully request that the present claims be advanced to allowance and issuance.

Applicants believe no fees are due in connection with the present filing. However, the Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment of the same, to Deposit Account No. 50-1774, Ref. No. CST-138 CIP.

The present claims are believed to be in condition for immediate allowance. Early and favorable consideration leading to prompt issuance of these claims is earnestly solicited. If there are any questions regarding these amendments, the Examiner is requested to call the undersigned attorney at the telephone number provided.

Respectfully submitted,



James Gregory Cullem, Reg. No. 43,569  
Intellectual Property Counsel  
CELL SIGNALING TECHNOLOGY, INC.  
166B Cummings Center  
Beverly, MA 01915  
(978) 867-2311

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Marked-Up Version of Claims

19. (Amended) A method for profiling modified protein levels or post-translational modifications in a cell on a genome wide scale, said method comprising the steps of:

[(a) generating at least one motif-specific, context-independent antibody against a conserved substrate motif, wherein said motif is selected from the group consisting of an unmodified substrate motif and a modified substrate motif;]

(a[b]) preparing an extract of [said] at least one cell; and

(b[c]) utilizing [the antibody of step (a)] at least one motif-specific, context-independent antibody according to claim 27 to profile the levels of [one or more] a plurality of proteins [containing said motif present] in the extract of step (a[b]) that contain said motif.

21. (Amended) [A] The method of claim 19, wherein said [for profiling] changes in modified protein levels or post-translational modifications [in a cell on a genome wide scale which] result from drug treatment, [, said method comprising the steps of:

(a) generating at least one motif-specific, context-independent antibody against a conserved substrate motif, wherein said motif is selected from the group consisting of an unmodified substrate motif and a modified substrate motif;

(b) preparing an extract of a cell treated with said drug; and

(c) utilizing said antibody of step (a) to profile changes in the levels of one or more proteins containing said motif present in said extract of step (b).]

22. (Amended) The method of claim 20 or 21, wherein said motif [of step (a)] is selected from the group consisting of [phosphothreonine, phosphoserine] MAPK [substrate] consensus substrate motifs [sites], 14-3-3 [consensus] binding motifs [sites], CDK [substrate] consensus substrate motifs [sites], PKA [substrate] consensus substrate motifs [sites], Akt [substrate] consensus substrate motifs [sites] and acetylated lysine.